



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Rama Ranganathan et al.

Serial No.: 09/684,066

Filed: October 6, 2000

For: STATISTICAL METHODS FOR
ANALYZING BIOLOGICAL
SEQUENCES

Group Art Unit: 1361

Examiner: Clow, L.

Atty. Dkt. No.: UTSD:645/MTG

DECLARATION OF RAMA RANGANATHAN

I, Rama Ranganathan, declare under penalty of perjury that:

1. I am over 18 years old and have personal knowledge of the facts below.
2. I am an Associate Professor at the University of Texas Southwestern Medical Center. I have held the title of Associate Professor for 1 year. I was an Assistant Professor for the preceding four years. I am also an Associate Investigator of the Howard Hughes Medical Institute, and have held that position for 1 year. I was an Assistant Investigator for the preceding four years.
3. In both capacities, 90% of my time is devoted to biological research. The remaining 10% of my time is devoted to teaching and other academic administrative duties.
4. I received my BS in engineering from Berkeley, and my MD and PhD degrees from the University of California, San Diego.
5. I am an inventor of this patent application.
6. I am familiar with Volume 266 of Methods in Enzymology (©1996) entitled "Computer Methods in Macromolecular Sequence Analysis." This work is dedicated to the process of creating MSAs and to the application of prior established methods operating on MSAs. Section III of this work, entitled "Multiple Alignment and Phylogenetic Trees," which is attached as exhibit A, addresses MSAs of polymers sequences such as proteins and DNA.
7. Other works that address protein MSAs include "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs" by Altschul *et al.*, *Nucleic Acids Research*, 1997, Vol. 25, No. 17, pgs. 3389-3402 (ex. B); and "SCOP: a Structural

Classification of Proteins database" by Hubbard *et al.*, *Nucleic Acids Research*, 1999, Vol. 27, No. 1, pgs. 254-256 (ex. C). Works that address RNA MSAs include "The Ribonuclease P Database" by Brown, *Nucleic Acids Research*, 1999, Vol. 27, No. 1, pg. 314 (ex. D); "tRNAscan-SE: a program for improved detection of transfer RNA genes in genomic sequence" by Lowe *et al.*, *Nucleic Acids Research*, 1997, Vol. 25, No. 5, pgs. 955-964 (ex. E); "Conservation of functional features of U6atac and U12 snRNAs between veterbrates and higher plants" by Shukla *et al.*, *RNA* (1999), 5:525-538 (ex. F); and "The uRNA database" by Zwieb, *Nucleic Acids Research*, 1997, Vol. 25, No. 1, pgs. 102-103 (ex. G).

8. Methods discussed in Volume 266 have been fundamental to a recognition of sequence homology as implemented in the BLAST® family of search tools, many of which – including versions of BLAST and PSI-BLAST (which also actually create alignments) – have existed in the art for more than 6 years; to the creation of phylogenetic trees since prior to October 6, 1999; and have been routine in the practice of molecular biology for guiding experimentation since prior to October 6, 1999.
9. Alignment methods are introduced in the required coursework for many biology graduate students, and have been since prior to October 6, 1999.
10. Interactive practical education in advanced methods have also been routine for upper-level bioinformatics graduate students since prior to October 6, 1999.
11. In my opinion, the skill required to create MSAs that may be accessed consistent with the "accessing" step of claim 1 of my application is no greater than that which is the standard of practice in the bioinformatics community.

Signed: _____

Dated: 4-7-2003

Name: _____

RAMA RANGANATHAN

Title: _____

ASSOCIATE PROFESSOR